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BNMPS: BIOMOLECULAR NANOMACHINE PROTOCOL STACK FOR HUMAN DISEASE DIAGNOSES: A NEW PARADIGM

FASEE ULLAH[1], AND IMRAN KHAN[2]
[1]Department of Computer Science, Abasyn University, Pakistan
fasee.ullah@abasyn.edu.pk
[2]Department of Computer Science, Abasyn University, Pakistan
Imran.khan@abasyn.edu.pk

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ABSTRACT. *Nanotechnology have many potentials to be used in various research directions for humanity. It is being used in many applications and products nowadays. One of the important application directions for this emerging technology is biomedical science and human body diagnosis. Nanomachine technology is part of the field concerning about creating and maintaining Nanoscale machines capable of performing certain functionalities such as molecule counting [1], molecule shuttling [2] and molecule sensing [3]. Communication between Nanomachines adds more capabilities and allows cooperative and distributed functionalities and form the concept of NanoNetworks [4]. Today's researchers are trying their best to deploy Nanomachines and NanoNetworks for real-time objectives such as medical purposes. Moreover, the same problem is faced in other fields such as battlefield networks, environmental monitoring, and automation fields. However, due to design issues of Nanomachines such as low computation capability, low processing power, limited storage, imperfect sensing, actuation, and limited networking capabilities, the work done in the field of Nanonetwork communication is inadequate.*

In this paper, we present a novel communication protocol stack model for Nanomachines and show how this model can be used in medical applications for human body diagnoses. Our model provides guidance regarding designing protocol stacks for Nanomachines.

Keywords*:* Nanomachine; NanoSensors; Protocol Stack; Communication; Vesicle; Membrane layer; Molecular Motor.

1. **Introduction.** According to Feynman, "There's Plenty of Room at the Bottom ..." [22]. For us, this means that there are many hidden things which exist in nature for communication that are still unknown and that will require more research work to understand them. However, these things make communication feasible between two communicating entities. For example: Air particles uses particles for communication. Until recently, nobody knew about the Nanomachines technology and its communication paradigms sending messages between two entities, like particles of air moving in arbitrary direction to send mes sages. Nanomachine communication coverage ranges from a few hundreds to thousands of nanometers regarding the deploy ment of objectives. Nanomachines offer services of computing, data storage, sensing and actuation [4]5][6][7][8][12].

Nano is a new and emerging technology in the biomedical sciences. This emerging field contains much potentials to be used in various ways for the benefit of humanity. Therefore, Nano's built Nanomachines consist of atoms. Various research labs have tried to use these Nanomachines for humanity medical treatment

purposes. Due to these reasons, aim of this paper is to introduce new protocol stack model for Nanomachines with distinguished features and compare this model with existing protocol stack models. This paper discusses a case study in which a proposed protocol stack model for Nanomachines is used in diagnosing patient problems and delivering medicines to specific parts of the human body. The other objective is to discuss proposed protocol stack model due to the lack of standardization of the protocol stack models for Nanomachines without validation of the system. The existing protocol stack models for Nanomachines do not have as many functionalities as the OSI model presented. The proposed protocol stack model contains new functionalities, such as packet (medicines) prioritization, packet queuing, & de-queuing, Error and Flow control mechanisms.

Our proposed protocol stack model for a Nanomachine is based on molecular communication and explains layering concepts for Nanomachine communication. This molecular communication further explains that Nanomachines require some propagation techniques and layering concepts and explains how these messages are encoded, routed, de-coded, and put on the physical membrane. This is another challenging issue. The reminder of this paper is constructed as follows. Fundamentals of the Nanomachines is included in section 2. Work related to existing problems is included in Section 3, while a proposed protocol stack model for Nanomachines is presented in Section 4. A comparison of existing and proposed stack models is presented in Section 5. The application of the proposed protocol stack model is included in Section 6, and conclusions & future work are in Section 7.

2. FUNDAMENTALS Of The Nanomachine :

The Nanomachine is a device comprised of small atoms which are used for interaction purposes in order to improve human life. The construction of these kinds of atoms requires rearranging them into molecules for communications, which is technologically very difficult. Therefore, various research activities are being applied in order to make Nanomachines feasible. The architecture of a Nanomachine with added functionalities includes the nanosensor, nanoactuator, nano-memory, nanoantenna, nano-EM transceiver,nano processor, and the vital nano power unit [5]. Most of the properties of Nanomachines have inherited from the sensor machine, including the capability of investigating the environment, sensing specific information in the environment, and responding to a particular part of the environment. Due to these capabilities, the Nanomachine is the most extended version of a sensor. However, communication patterns of Nanomachines are different and based on molecular communication and electromagnetic communication patterns.

Nanomachine has three functional units for message sending and receiving which are Emission Process, Diffusion (Propagation) Process and Reception Process [8][12]. Through the Emission Process, a sender node generates messages (signal). However, before sending these messages to the Reception process at Receiver Node, the messages are converted into a specific pattern and forwarded to the propagation process, which works as a medium that receives these messages as input and forwards them to the reception process. On the receiving side, the reception node reverses the process with respect to the Emission Process that reads the message. This propagation process needs more elaboration for optimized sending and receiving of the messages.

Traditional communication shows various communication types with different input and output directions. However, wireless communication is being one of them. The Nanomachine therefore has also three different types of communication units, including a physical Nanosensor, a chemical Nanosensor and a biological Nanosensor [5]. The physical Nanosensor measures magnitude, such as pressure, temperature, and force, while the chemical nanosensor measures gas, specific types of molecules, and the composition of molecules. However, biological nanosensors are totally different. They monitor biomolecular processes such as DNA interactions and cellular communications. Applications for these three types of nanosensor machines are unlimited. We are considering potential applications such as human body medical diagnostics and environmental monitoring based on event detections.

NanoSensors are being used in various heterogeneous environments of critical operations such as patient diagnoses that needs more work to change the design of the NanoSensor machine. Therefore, it has design restrictions which affects architecture, such as low storage capacity is an issue when the memory unit consists of 5x5x5 atoms = 125 Atoms. A single bit of information is stored in a single atom [5][12]. Mechanical energy, vibrational energy and hydrualic energy generation mechanisms are alternate approaches used to recharge a battery of the Nanosensor [5].

The Nano-Electromagnetic Communication type defines that messages are exchanged between communicating Nanoma chines, with the help of electromagnetic radiation. This type of communication is

specially designed for long range distance communication such as Carbon Tubes [7]. Meanwhile, Molecular Communication type defines how the messages are exchanged between communicating Nanomachines with the help of Molecules. Walkway, Flow and Diffusion [5] are defined and based on the main type of Molecular Communication. Walkway based Molecular communication defines pre-defined schedules with pre-defined paths for carrying molecules, while Flow based Molecular communication gives guidelines and predications to carry molecules. A relevant example to Flow based molecular communication is that we can easily differentiate various human voices. The Diffusion based Molecular communication is different and shown in Fig 1.

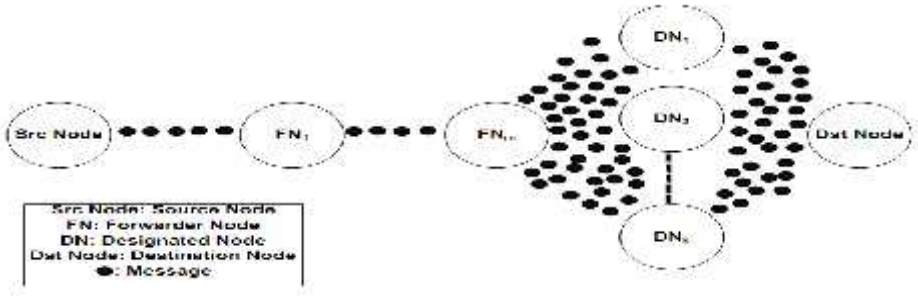

Fig1: Diffusion based Molecular Comunication

In Fig 1, FN (Forwarder Node) is comprised of m number of nodes and received molecules (messages in small black dots) from source node (Src Node) and the FN (from 1 to m number of nodes) nodes forwards them to the destination. FN1 will ematical equations show how the Source Node will forward molecules to the Destination Node through intermediate nodes as follows.

Src Node = FN1 + ... + FNm
FN1 + ... + FNm = DN1 + ... + DNk
DN1 + ... + DNk = Dst Node
So all these mathematical steps can be written in one step with working approaches as follows.
Src Node=FN1 + ... + FNm + DN1 + ... + DNk + Dst Node

1. First, The Src node (Source Node) will forward molecules to the FN1 Node and the FN1 Node will then forward them to the FNm Node. The FNm will send an “ADV” (Advertised) message to all next directed hops such as DN 1 to k nodes.
2. If any DN (Designated Node) is required to receive and forward molecules to the destination node then any DN will reply back with an ACK message method to show willingness and then DN will receive molecules from FNm because every DN node has complete information of the routes of the network(s).
3. The FNm will forward molecules to interested DN nodes and DN nodes will forward molecules (small black dots) to the destination. In this way the molecules will reach the Dst Node (Destination Node) with the help of hop by hop counting. Most of the literature reviews show topologies concepts for information gathering on surrounding, forwarding & receiving and are depicted in bus, star, spiral [9] and grid, hexagon, and T shape [10] topologies.

3. **Related Work** Securing Nanosensor machines communication is the primary and the very complex task of the protocol suites. We know it from the very beginning how the TCP/IP protocol suite works layer by layer regarding communication level and security aspects. In Nano Molecular communication, the communication environment is different from existing communication environment of the TCP/IP protocol suites. Suggestions provided in prior research are inadequate, so, more efficient work is required to determine a method for analyzing, designing and simulating a Nanomachine protocol stack. Currently, Nanotechnology is in the learning stages and requires more time in order to develop an innovative model for practical applications.
Currently, it is not feasible to implement the TCP/IP protocol suite on the Nanomachine due to inadequate memory storage, low processing power and low sensing capabilities. However, the authors of [11] present protocol suite for Transmitter and Receiver, which has the same number of layers (Application, Transport,

Network and Physical layers) presented on both sides of the nodes. Each layer contains different types of services that are applied on Nanomachine. Application layer contains interfaces and message formation; Transport layer provides integrity and encoding services, and the Network layer performs the process of packets injection and the end to end delivery of packets. The physical layer is the final layer in which the packets are injected. This layered protocol stack is used in medicines and specialized for life-saving, efficient drug delivery.

However, the authors [11] do not follow the basic communication mechanisms of Nanotechnology processes, such as DNAs, Enzymes and deployments because Nanotechnology contains several communication mechanisms, including short-range, medium-range, and long-range communication. Therefore, human treatment requires additional dedicated work in processing of various medicines. The design of TCP/IP is suitable for existing machines in the capacity of high processing, high storage and quick decision making, but implementation of all layers of the TCP/IP protocol suite on the Nanomachine is not feasible due to lack of simulation and validation for practical applications. It also requires high processing speed and high storage capacity.

Information sensing, gathering and processing from multiple nodes is handled by inverter and NAND gates [14][15][16], which requires some molecular logic gates in order to store one bit of information in a single atom (where 5x5x5 atoms stores 125 atoms of information) [5][22].

Knowledge configuration and handling in molecular based multiple Nanosensors communication is inadequate. However [13] presents theoretical concepts for handling multiple nanosensors communications on existing TCP/IP layers with distinguished features such as biocompatibility, scalability and information representation. Some of the other specific types of biological communication include intracellular transport, intercellular communication, homeostasis and bacterial conjunction for molecular motor that move and convert chemical energy into mechanical works.

The Microtubule is a molecular motor that consists of two types: Vesicle (type of message) Kinesin motor and Vesicle Dynein motor, which are used for sending and receiving messages respectively. The communication mechanism inside molecular is based on Sink (Base Station), in which the sender sends messages first to the encoder / decoder node under the supervision of sink and then to the destination according to communication polices adopted. This scenario explains a single-hop communication; however, the establishment of multi-hop communication among nodes presents major complexities for managing addresses and feedback acknowledgements for a sender as well as a sink.

TCP/IP layer for molecular communication is based on the Vesicle (number of messages divides into fixed form) for comparison between molecular motor and brownian motion [17]. Brownian motion is a random movement of particles in a gas or fluid, in which the particles are subjected to continuous collision with surrounding molecules from all directions. Further more, this paper also explains that molecular communication consists of Loading zone and Unloading zone. The loading zone carries molecules towards receiver and unloading zone drops molecules on the receiver side. The microtubules plays an active role for a communication medium and transport binary numbers from the loaded zone to the unloaded zone with the following configurations such as“00” for 0 vesicles, “01” for 1 vesicle, “10” for 2 vesicles, and “11” for 3 vesicles [17] respectively. Adhoc Network concepts is used for message authentication between Nanomachines through multi hops with the help of molecules [18]. For this purpose, a protocol stack model is presented with the main features of message encoding & error recovery on the sender side while on the receiver side, message decoding & error recovery with molecular scheme are presented. The Protocol stack model is implemented on Nanomachine with features such as application layer is being used for encoding and decoding. The Transport layer is used for Transmission and Error Recovery. The Application layer has compartments, and each compartment has sub compartment that provide logical functions in order to draw logic circuits for communication. However, they also refer Stetter et al [19] solutions to the error recovery of addresses with finite state machine.

A biological based protocol stack model suggest some modules for Nanomachines as shown in Fig 2 [20] such as application interface, link switching and physical (membrane) layer considers a protocol stack model for Nanomachine. In this protocol stack, they prioritized the data into two types: Sensory data which has a low priority, and command data with high priority instructions. However, inadequacies in designing, modelling and simulation prevent validation of the system. The Fig 3[21] has same functionalities as shown in Fig

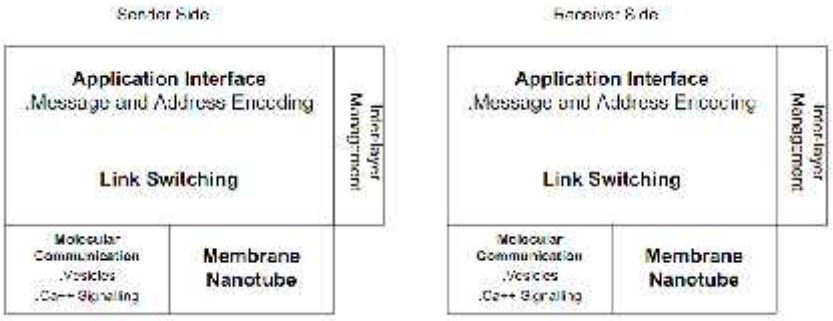

Fig.2. Components of Molecular Communication Protocol Stack[20]

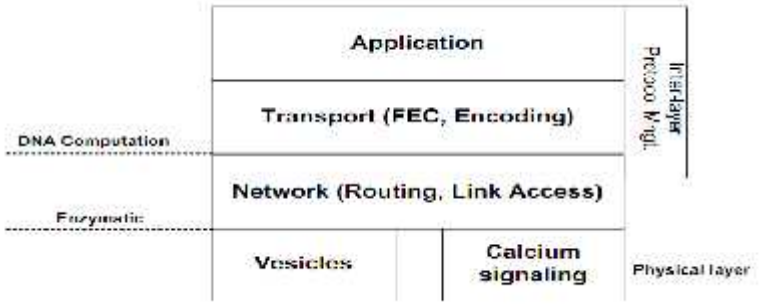

Fig. 3. Protocol Stack for Molecular Communication [21]

2[20], excepts, DNA, & Enzyme Modules, Transport, and Network layers are presented. This protocol stack model breaks down into two main types: DNA and Enzyme. DNA provides superior, rapid communication with less engineering work while Enzyme is used for the creation of logic gates with simple computations. The Transport layer provides encoding of the messages and Network layer provides routing alongwith link access control.

4. **Proposed Protocol Stack Model for NanoMachine** The TCP/IP is good layering concepts which is used for heavy machines such as desktop computers, laptops, an smartphones. The authors of [11] presented TCP/IP layered communication protocol for Nano communication. However, the implementation is not feasible for tiny Nanomachines due to low processing, low memory storage and low sensing functionalities.
This paper presents the functionalities of proposed protocol stack model and compared with existing models as follows.

i. **Encoding and Decoding of a message**: Securing messages during transmission is the important task to keep them protect from unauthorized access. Due to this security reason, the proposed protocol stack model is shown in Fig 4 that provides functionalities of the Encoding and Decoding to keep messages secure. However, in Fig 2[20] and Fig 3[21] contain only encoding function. On the receiver side, there is no decoding scheme is presented in the existing models but in the proposed work contains the functionality of the decoding of the message on the receiver side.

ii.Queue and Dequeuing of a message: The messages storage for short interval time is presented in the Queue and Dequeue processes. The purpose of this layer is that Nanomachine is busy in the other parts of the human body to detect malfunctioning parts in it and in order to hold messages for a moments not to interrupt the flows of Nanomachines.

iii.Packet Prioritization and Routing: In communication, there are two paths exist for efficient communication such as low priority packet data delivery and high priority packet data delivery with high bandwidth routing paths are presented in Fig 4. The authors of 2[20] is defined routing function but do not include packet prioritization technique and same in Fig 3[21] also do not define both functionalities.

iv. Error and Flow Control: There must be some mechanism to control the speed of packets of the sender

not to crush the bandwidth of the network and also not to crush the buffer of the receiver during communication of Nanomachines is the aim of the proposed protocol stack model. So two unique features are used for detecting of error and controlling of flow such as error control and flow control respectively. The aim of these two mechanisms are to avoid any kind of message loss and bandwidth of the network. This unique feature is not included in the existing models of the Nanomachine protocol stack.

v. Nano Membrane, Molecular communication, Vesicle etc: The message propagation requires communication mediums such as in wired based communication, it needs a fiber optic etc and in wireless communication, it needs signals for a message propagation. However, in biomedical characteristics, Nanomachine needs Nano Membrane, molecular motors, calcium, vesicle etc are the types of the message propagation included in all available existing models and also presented in proposed protocol stack model.

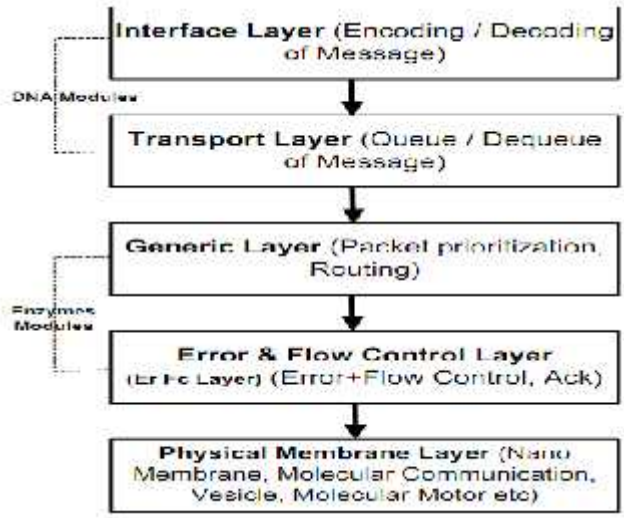

Fig. 4. Proposed Protocol Stack model for molecular communication of Nanomachine

These are the functionalities of the proposed protocol stack model as shown in Fig 4 for Nanomachines and also compared with existing protocol stack models as shown in Fig 2[20] and Fig 3[21].

The functionality of the proposed protocol stack model explained and now these functionality assign to each layer of the proposed protocol stack model as follows.

- Functionalities of encoding and decoding of messages explained and these functionalities assign to the first layer of the proposed protocol stack model that is interface layer. Interface layer provides interfaces to read (e.g. capture) and write (e.g. broadcast) information between communicating Nanomachines. Before reading and writing operations on the data, it must encode and decode as per the communication policy stated for deployment. For example: if Nanomachines deploy in battle field environment then how they will read the information from battle field securely is a significant tasks, or, if they deploy in the human body then how they will deliver a specific medicine to a specific part of the human body, or how they will deploy, read and configure information for smooth functionality is important. In order to achieve these targeted results, we divide the human body into four specific parts to clearly identify the problem(s) or directly diagnose the problems of a specific part of the body (e.g. X1) as shown in the Fig 5. The interface is not like an application layer. However, it provides a communication infrastructure for the Nanomachines.
- In communication, data or messages require to divide into small chunks before sending. On the receiver side, these chunks should combine to read a complete message. These kind of functionalities are always provided by transport layer. This layer offers services of transportation and information storage of high and low priority data for sending and receiving purposes. This layer has also the robust feature of queuing and dequeuing processes. For example, if a Nanomachine is busy in executing a process in Z part (in Fig 5) of the body then the transport layer will not interrupt and stop this ongoing process to achieve targeted results, and at the same time if new process is born so it will be stored in a queue/Dequeue location of a transport layer for efficient and smooth interaction inside the body.

- Some applications need a dedicated path to send and receive messages. This kind of functionality can be provided by a Generic layer. This generic layer has unique feature of being able to carry packets machine to machine (1:1) and machine to multiple machine (M: N Broadcast). In an emergency cases, a generic layer selects the best path in the capacity of shortest and longest paths by using hop counts. For this path selection process, the gap junction and diffusion methods are used with the help of direct access and indirect access [23]. For example, sometimes a Nanomachine is busy in detecting malfunctioned units in the body and at the same time a doctor or user instructs Nanomachines to perform a specific task inside the body. So in this critical situation, priority is assigned to the specific task to accomplish the results. Other features of the generic layer are interoperability and multiple environments (human body, military operation, vehicle detection, etc.).
- To maintain the integrity of the data during transmission is need a mechanism which provides protection of data from error and also provides to limit the speed of messages. For medication objectives, this layer is Er Fc layer where Er and Fc stands for error correction and flow control of the sender respectively and also informs the receiver about error & flow control issues. For example, a doctor diagnoses X1 part (subpart of X) of the body with some medication solutions. During this process, and at the same time, other parts of the body also request new input (medication) for the same problem (e.g. say X1) and a doctor is still forcing X1 part (shown in Fig 5) to accept more instructions or medicines. In this critical situation, we have an Er Fc control mechanism that periodically participates to control the flow of the sender by returning acknowledgement "ACK" to the sender. It also informs the receiver (X1) that the sender has created an overflow issue, while Er maintains proper execution of the medicine in the specific part of the body, the purpose is whether the medicine has properly reached to the destination. This is one of the vital roles of nano practices. Sometimes a human body is affected by more than one disorders and different specialist doctors prescribe different medicines for different parts of the body in order to help and recover from these disorders.
- Cell-based molecular communication needs physical layer which comprise of physical membrane. For this purpose, most of the literature reviews present a technique called gap conjunction (e.g. Ca2+, IP3) [24]. The Gap junction is a combination of communication gates or channels in the cells and is used to establish a direct connection for a guided media.
  A gap junction can be used when a sender and a receiver are far apart and are not able to reach each other. In this case, using an indirect method like gap conjunction directly connects the cytoplasm of two cells and enables them to send and receive molecules. For wireless communications (unguided media), cells diffuse signal molecules (e.g., ATP, cyclic AMP). These techniques are used in the extracellular environment, and nearby cells respond to the molecules (paracrine signaling) [24]. In this way a communication channel is established between two communicating nanomachines. The proposed protocol stack model uses both communication techniques to forward and receive messages that depend upon the environment of communication which is known as **Physical membrane layer**.

The provided functionality explained in detail and each functionality has assigned to each layer of the proposed protocol stack model of Nanomachines as shown in Fig 4. Now, our final task to group these layers according to the biomedical characteristics and assign biomedical terms. The interface layer and transport layer are grouped to the DNA module because DNA molecules are long in shape and can work as long packet to carry data. The DNA is also used for message encoding and decoding.

The generic and Error & Control layers are grouped into the Enzyme module. Enzymes are kinds of proteins that can use as logical gate as a communication medium for Nanomachines. Enzymes can use to control the flow of the packets (Routing) and provides error and flow control of the medium.

The Physical membrane is a combination of various tissues related to message propagation functions such as vesicles etc. These grouping of the layers, defining layers and assigning functionalities to each layer is to clearly understand the objectives of the proposed protocol stack model. The molecular communication architecture presents in [25], and our proposed protocol stack model has designed in a way that executes the sending and receiving of messages with the features of encoding, decoding and message filtering.

5. **Comparison of Protocol Stack Models** Two protocol stack models presented in Fig 2[20] and Fig 3[21] respectively. Our proposed protocol stack model (shown in Fig 4) compared with Fig 3 [21] due to inadequate functionalities provided in this existing model.
In this paper, our contribution is to define the functionalities of each layer and divide them into three main modules (DNA, enzyme and physical membrane). In Fig 3[21], there are four layers with provided functionalities, and the proposed stack model has five layers with distinguishing features. An extra header added to the existing protocol stack model as shown in Fig 3[21] for controlling the management and execution of the functionality of each layer. However, the proposed protocol stack has no extra header because maximum functionalities have covered in each layer and extra overhead of management and execution of the functionalities has removed.

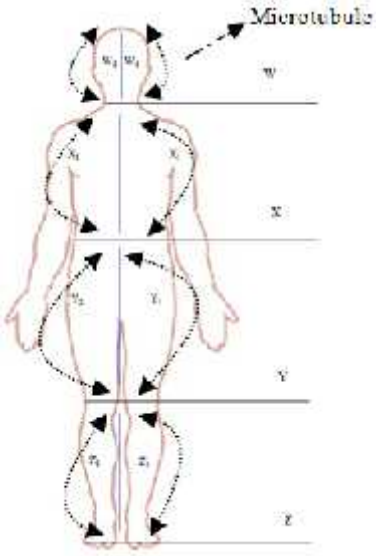

Fig. 5. Protocol Stack uses on Human Body. Division is performed due to complexity level of the human body. The doctor instructs the molecules that should reach to the mentioned part of the body and executes on it. The Arrow signs show Microtubules and these are used as medium for executing medicines in each portion (e.g. X1 or X2 etc) of the body.

The existing protocol stack models are shown in Fig 2[20] and 3[21] and the proposed protocol stack model is shown in Fig 4 and their functionalities compared in Table I. We noticed table I, most of the functions covered in the proposed model and many functions not covered in the existing models. In Table I, the boldface text shows functionalities of the proposed protocol stack model while italic text shows functionalities of the existing protocol stack model, and functionalities in underlined text is contained in both models.
The functionalities of both existing and newly proposed protocol models shown in the services column of Table I. However, strengthened functionalities of the proposed protocol stack model are: reading/writing, Encoding/Decoding, queuing/dequeuing, packet prioritization and assigning the best path, error and flow control, and the physical membrane. These features compared to the existing model. Based on this comparison, we can clearly demonstrate that our proposed protocol stack model is adequate and efficient for patient diagnoses and drug delivery system.

6. **Application of the Proposed Protocol Stack Model** Our proposed protocol stack model as shown in Fig 4 is suitable for medical diagnoses and tried to implement them, as seen in Fig 5, in which a human body grouped into various parts based on levels of complexity and molecules can swap from one part of the body to another. The functionalities of each layer is described as follows.

Application of the Interface Layer The purpose of this human body division is to focus on specific parts of

the body and identify the problem such as (e.g. X1). Interface layer gives functions of messages encoding and decoding with read and write operation on data such as, how the Nanomachines will deliver a specific medicine to a specific part of the human body as shown in Fig 5, or how they will deploy in the human body.

Application of the Transport Layer if a Nanomachine is busy in executing a process in Z part (in Fig 5) of the body then the transport layer will not interrupt and stop this ongoing process to achieve objectives, and at the same time a newly-born activity will be stored in a queue/dequeue location of a transport layer.

Application of the Generic Layer In an emergency situation, a generic layer selects the best path in the capacity of shortest. For this path selection process, the gap junction and diffusion methods are used with the help of direct access and indirect access [23].

Applicaton of Error and Flow control layer Handling communication between a doctor and patient need a controlling mechanism to fix the things between them. For example, a doctor diagnoses X1 part (subpart of X) of the body with some medication solutions. During this process, and at the same time, other parts of the body also request new input for the same problem (e.g. say X1) and a doctor is still forcing X1 part (shown in Fig 5) to accept more instructions or medicines. In this situation, we have an Er Fc control mechanism that periodically participates to control the flow of the sender by returning acknowledgement "ACK" to the sender. It also informs the receiver (X1) that the sender has created an overflow issue, while Er maintains proper execution of the medicine in the proper location. The Fig 4, Fig 5 and Table I are clear justification for the proposed protocol stack model as compared to existing models.

Functions	Layer	Module	2[20]	3[21]	[Fig 4]
Encoding & De-coding	**Interface**	**DNA**	Not Applicable	Not Applicable	**YES**
Encoding	Application Interface	DNA	Not Applicable	YES	Not Applicable
Queue & De-Queue	**Transport**	**DNA**	Not Applicable	Not Applicable	**YES**
Packet Prioritization, Routing	**Generic**	**Enzymes**	Not Applicable	Not Applicable	**YES**
Routing Link Access	Network	Enzymes	YES	YES	Not Applicable
Vesicle, Calcium etc	Physical Membrane	YES	YES	YES	YES

Table1: Comparison of Functions of Protocol Stack Models

7. **Conclusion with Future Work** Nanotechnology is in the initial stages and needs more time to become mature in the coming decades. Communities related to nanotechnology are trying their level best to design molecular-based communication infrastructures. Our proposed protocol stack model has demonstrated descriptive solutions with medical diagnostic features.
After successfully testing this model, it could be very useful in medical fields. However, there is no proper instrument or tool available for testing to validate and achieve real-time objectives and practical applications for humanity.

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